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PRINCIPAL INVESTIGATOR: Patricia Dischinger, Ph.D.

CONTRACTING ORGANIZATION: University of Maryland, Baltimore
Baltimore, MD 21203-6428

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13. ABSTRACT (Maximum 200 Words) The purpose of this study is to identify a cohort of patients with mild Traumatic Brain Injury and follow them for 1 year post-injury to determine injury outcomes and identify factors that best predict long-term sequelae. The first year has been dedicated to finalization of study design and testing instruments, and logistical planning for this multi-disciplinary effort. Staff were hired and trained, and a manual of operations developed to standardize the protocols for evaluation components. A schedule for testing was developed, and enrollment criteria defined. Human subjects approval was obtained from both the University and Army review boards. Space was located within the Trauma Center for patient testing, and equipment moved and calibrated. A database was created for each of the evaluations, including a process for data back-up and migration. Laboratory protocols were developed for the collection, storage, and processing of blood samples for the S-100b tests. Actual recruitment began in October 2003. After an initial pilot phase it was determined that, although sufficient numbers of patients with mild TBI were admitted, a variety of issues have impacted recruitment. Based on this experience, protocol modifications are planned in order to correct the problem and enhance patient enrollment.				
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INTRODUCTION

Each year approximately 1.5 million Americans sustain a traumatic brain injury (TBI). The most common causes of TBI are due to blunt force trauma. The goal of this research is to identify a cohort of patients with mild TBI and follow them for a period of one year (1) to determine injury outcomes and (2) to identify those factors that best predict those patients with long-term sequelae. A sample of 300 subjects will be identified over the life of the study. These subjects will have a baseline assessment during the initial trauma center admission which includes biochemical markers, balance measures, clinical findings and neurometric tests. Follow-up testing will be completed at 3-5 days, 7-10 days, 3 months, 6 months and 12 months post injury.

BODY

This is the annual report for year 1 of a 3-year study. The first year focused on setting up the study and making decisions about the logistical operations of the various components of the study with the multidisciplinary research team.

Human Subjects Protections:

Finalizing the human subjects aspects of the study required more time than originally anticipated. The University of Maryland, Human Research Protections Office (HRPO) classified the study as minimal risk and the Human Subjects Research Review Board (HSRRB) at the Department of the Army classified the study as high risk. After much discussion and email correspondence, it was determined that the HSRRB would not approve the study unless HRPO designated the study as high risk. With several modifications related to study classification and other minor issues, both the HRPO and the HSRRB approved the study protocol in July 2003.

In anticipation of being funded for this research endeavor, we applied for the Certificate of Confidentiality in January 2003. The Certificate was received in March 2003.

Each member of the research staff was required by the HRPO to complete Human Subjects and HIPAA training. This effort was coordinated by the clinical research coordinators.

Hiring New Personnel:

Two part-time clinical research coordinators were hired during the past year. They are responsible for the day-to-day functioning of the study. This includes, but is not limited to the following; screening and recruiting subjects, coordination of initial evaluations, performing certain aspects of the initial evaluation, scheduling, coordinating and performing follow-up evaluations, entering and editing data collection. The coordinators are also responsible for training other personnel on various aspects of the study and making sure all certifications are up to date.

Staffing / Training:

In addition to the clinical research coordinators, Physical Therapists and Speech and Language Pathologists from the University of Maryland Medical Systems (UMMS) Rehabilitation Services Department are also part of this study. During this past year much time was spent working out the logistics of coverage for the study. This included compensation as well as training. Part of the training was to ensure inter-rater reliability among staff performing various tests, especially the balance components. A Neuropsychologist from the Baltimore VA Hospital was recruited to perform computerized testing and cross-training of the research coordinators for the ARES (Automated Neuropsychological Assessment Metrics {ANAM} – Readiness Evaluation System) component of the evaluation. Non-clinical members of the study staff were also trained to assist with balance testing as a “spotter” to ensure subject safety.

For licensed therapists performing evaluations as a component of the study, professional liability issues also needed to be addressed. Determination of hours worked being paid to the Rehabilitation Services Department, or directly to the therapist had an impact on their individual professional liability coverage. This necessitated the development of a new job description to ensure coverage for therapists when they were compensated directly for study activities

Safety:

Because this research endeavor involves hands on contact with subjects, there were various safety assurances that had to be met. First, anyone performing evaluations had to provide up to date CPR documentation. Next, the office used for testing had to be inspected by the UMMS safety office. Policy and procedures for handling arrest/ patient care issues had to be developed and reviewed by members of the hospital medical staff. Since safety measures needed to be established for both subjects who were still inpatients as well as returning for follow-up visits, a decision tree was created to aid in appropriate notification of medical staff in the event of an adverse response to testing. Supplies essential to maintaining the safety of the subjects were procured, including oxygen tank and supplies, gait belts/harness system for balance testing and blood pressure cuff and stethoscope. Notification of the hospital code team was completed as well and locating the closest hospital crash cart and posting of this information in case of an emergency situation. Safety measures also included the addition of two telephone lines into the testing office to allow for paging of staff in the event of an emergency. Safety for evaluators as well as subjects was also considered, and the need for two study staff to be present during evaluation is frequently warranted. A second staff member is present during all balance testing, most initial evaluations and during follow-up evaluations when there are multiple post-concussive symptoms reported, or subjects demonstrate personal space boundary issues.

Space Allocation:

Adequate space was located to house the Balance Master System, in addition to serving as a location for additional floor balance testing and all the cognitive testing. This space needed to be located near both the clinic waiting area for the convenience of subjects on

follow-up visits, and accessible to the trauma admitting area for completion of initial evaluations. The office space that was obtained also needed modification to allow computer set up for testing and data entry, adequate desk space for testing completion, adequate floor space to ensure safe completion of balance testing. The Balance Master System was moved from another location on the UMB campus and was calibrated by the manufacturer after the move. A biomedical check of the Balance Master was also completed by the hospital Biomedical Engineering department before use with subjects.

Manual of Operations:

An extensive manual of operations was created to ensure consistency and clarity for the numerous staff members working on and with the study. Policy and procedures were developed to cover the recruitment and follow-up scheduling of subjects, individual evaluation component procedures and reporting, and administrative tools. Subject specific policies include subject consent and authorization, overview information, storage and organization of subject files, safety procedures and adverse event reporting and subject compensation for participation. All policies and procedures were reviewed by the appropriate team members and matched to institutional and governmental regulations for consistency when appropriate. Master binders are kept in both the central study office and the satellite testing area for easy reference, and updated as necessary.

A resource manual containing relevant research articles, manufacturer instructions and keys for test interpretation was also created.

Test Development Schedules:

Finalization of the testing instruments to be used and the schedule of their administration required much discussion. Several initially proposed tools were unable to be utilized in the final analysis. The Modified Galveston Orientation and Amnesia Test was replaced with the original Galveston Orientation and Amnesia Test (GOAT), as the modified version had not yet been reported in the literature. The Symptom Checklist utilized was changed to a version providing more objective documentation of post-concussive symptoms including intensity and frequency of symptoms. The Computer Assessment of Response Bias (CARB) was removed due to proprietary issues.

Scheduling of testing also required discussion and modification during the first 6 months of year 1. The entire battery of tests requires between 2 ½ and 3 hours to administer. Determining the best sequence to achieve maximum subject participation required numerous trial sessions with study staff serving as subjects. Ultimately, while a desired sequence of evaluation components has been identified, subject tolerance and availability of subject (during initial assessment) and staff dictates the actual sequence. Ideal sequencing would have the interview and all cognitive components performed prior to balance testing. Subjects to date have expressed a need for a break in the cognitive testing (which can take up to 2 hours by the 3 month assessment), and performance of balance testing at the mid-point aids in effective completion of the entire battery of tests.

Team Meetings:

Meetings of the study team to review and finalize all assessment tools, schedules and plans were held every two to four weeks during the first 6 months of the year, and

monthly thereafter. Additional small group meetings were held as needed for training and standardization of approach.

Specific meetings were held with physician and nursing leadership prior to the initiation of recruitment to orient them to the study and the role they would have in successful recruitment and management of patient care issues should they arise.

S-100 beta testing:

Meetings were held with members of the Trauma Stat lab and University Research Lab to devise the most effective method to obtain and store blood samples for the S-100b blood test. This process included development of procedures to ensure timely retrieval and freezing of blood samples per testing guidelines and moving of the samples to the research lab for storage until ready for bulk processing. Maintaining effective communication regarding samples, while protecting subject privacy was established and continues to be reviewed as needed.

Data Entry and Storage:

Access database forms and a data back-up process were developed for each of the evaluation components delivered via paper and pencil. A process for data back up and migration to an Access database was developed for the computer-based tools (ARES, ANAM). Training of research staff was completed for data entry and auditing, with expectations for data entry to be completed within 48 hours of each evaluation.

ANAM Proprietary Issues:

All study staff administering the ANAM or ARES were required to sign usage agreements as the software is the proprietary information of the USAMRMC. Software usage as well as data collection, storage and analysis will be consistent with the user agreement. In order to utilize these test batteries, 2 laptops and 5 palm pilots were procured for exclusive use with these tests.

Initial Recruitment Efforts and Modifications:

Recruitment has been considerably slower than anticipated, and after much discussion, we have identified several possible factors: (1) we began recruitment during the colder months of the year, when overall patient enrollment is down somewhat. However, large numbers of patients were still screened, but were not enrolled for various reasons related to our selection criteria, which were initially designed based on the assumption that all three aspects of the study had to be completed (i.e. the balance tests, blood test, and neuropsych testing). (2) Many patients were not eligible based on their associated injuries, such as upper and lower extremity injuries, which precluded their completing the balance test. These patients, however, are representative of the types of patients seen in trauma centers, who rarely sustain only one injury. (3) Others may have had only a mild TBI, but by the time clinical tests were completed, were unwilling to stay in the hospital longer in order to be enrolled in the research study. (4) Still others might have been eligible, were willing to participate, but expressed the fact that they would be unable to return for follow-up visits.

Based on these observations, we have made the following conclusions. There are adequate numbers of patients coming through the system with mild TBI, but we are losing many due to logistical considerations based on these "real world" issues. While the goal is still to obtain testing for all three study aspects, a more realistic approach might be to obtain as much data as possible for each enrolled patient. That is, if a patient has a lower extremity injury, but is otherwise able to participate, we will enroll him, obtain the blood sample and neuropsych testing, and request that he return for follow-up visits. If a patient is eligible, willing to return for follow-ups, but unwilling to stay for the initial two-hour battery of tests, we will obtain consent, basic intake data and the blood sample, and then notify him with regard to scheduled follow-up visits. For patients who are enrolled but do not return for specified follow-up visits, we will interview them by telephone using the symptom checklist.

Another possible consideration with respect to our sluggish enrollment to date is the fact that staff has not been available for screening during the evening and weekend hours. Therefore we have made arrangements for some weekend coverage, and also the possibility of "on-call" coverage in the evening, if the daytime research staff cannot complete enrollment.

We hope that this new approach, once approved, will allow us to still enroll the anticipated number of subjects. Analyses of those with all three testing aspects will provide a "core" database, and allow us to identify correlations between the tests. In addition, we will be able to compare characteristics of patients with the full battery of tests to those who could complete only two or one of the aspects, in order to determine if there are any biases.

Actual screening and recruitment was initiated on October 6, 2003. In the initial recruitment stage (10/6 – 10/20), issues related to potential subjects who lived outside the original geographical recruitment area and did not fit the age range were identified. Modifications were submitted to the IRB at UMB and the Army to expand the encatchment area to include 4 additional surrounding counties and increase the age of participants; as well as the aforementioned evaluation tool changes, and modification of the consent witness procedure to be consistent with HSRRB policy. These modifications were approved in November 2003. On January 30, 2004 additional modifications were submitted to expand the inclusion criteria by removing geographical boundaries and allow inclusion of associated injuries that did not require extensive medical management. These modifications were approved in March of 2004. The chart below summarizes progress to date in subject screening and recruitment.

As of 03/31/04 362 subjects were screened

14 Subjects recruited

- 8 complete Initial, 3-5 Day, 7-10 Day evaluations
- 4 complete Initial and either 3-5 Day or 7-10 Day evaluations
- 1 complete Initial evaluation then lost to follow-up
- 1 incomplete Initial evaluation then lost to follow-up

348 Subjects not recruited (detail as below)

Reason	#
Age	4
Non-local resident	26
No LOC, MS changes	72
MMS <8/10	4
Non-English speaker	8
Associated injuries	122
Discharged before screened	46
Refused	16
Penetrating	3
Other	43
Readmits	4

In April, Dr. Dischinger will be presenting a poster at the Department of Defense Military Health Research Forum, San Juan Puerto Rico, detailing the study overview and progress to date. A copy of the abstract may be found in the appendix.

KEY RESEARCH ACCOMPLISHMENTS

There are no key research accomplishments at this time. The research is in the early recruitment phase with limited data collection completed.

REPORTABLE OUTCOMES

Abstract Submitted and Accepted:

Dischinger PC, Cooper C, Mackenzie, Romani W, Spector J: Serial Assessment of Mild Head Injury: Early Predictors of Outcome, Department of Defense Military Health Research Forum, San Juan Puerto Rico, April 25-28, 2004

CONCLUSIONS

The research is in the early recruitment phase with limited data collection completed, thus there are no conclusions to be made at this time.

REFERENCES

None at this time, research is in early recruitment phase with limited data collection completed.

APPENDIX

ABSTRACT SUBMISSION

SERIAL ASSESSMENT OF MILD HEAD INJURY: EARLY PREDICTORS OF OUTCOME

Dischinger PC, Cooper C, Mackenzie CF, Romani W, Spector J

University of Maryland School of Medicine, Baltimore, MD 21201, USA

BACKGROUND/PURPOSE: The goal of this research endeavor is to identify a cohort of patients with mild TBI (traumatic brain injury) and follow them for a period of one year (1) to determine injury outcomes and (2) to identify those factors that best predict those patients with long-term sequelae. **METHODS:** Identify 300 patients with a mild TBI and obtain baseline measures including biochemical markers, balance measures, clinical findings and neurometric tests. Subjects will be followed at 3-5 days, 7-10 days, 3-, 6-, and 12-months post injury. **RESULTS:** We have only just begun patient recruitment and therefore have no results yet. By April, we should have preliminary findings available. **CONCLUSIONS:** The anticipated result is that biochemical and/or balance measures will add prognostic power to the prediction of long-term outcomes, and thus, could be used in the field to determine the disposition of soldiers who incur mild traumatic brain injury.